Breast calcifications: description and classification according to BI-RADS 5th Edition

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Abstract: Breast calcifications are a common finding in mammography. The majority of them have a benign origin, such as in the case of response to inflammatory disease of ducts or coarse calcifications in benign nodules. Many of these calcifications present a characteristic benign appearance and do not need to be magnified or monitored. However, other calcifications can occur grouped, have a suspicious-looking appearance and originate in a ductal carcinoma in situ or a high-risk lesion. It is important to know the morphology and distribution patterns of these calcifications in order to make appropriate decisions for each case. In the 5th edition of the BI-RADS Atlas, 2013, the categories and levels of suspicion of some patterns were modified. The aim of this article is to update the BI-RADS descriptors and categories for microcalcifications, indicating their most important features and the risk of malignancy associated with each descriptor.
Keywords: Microcalcifications; BI-RADS; Breast cancer

Introduction
Breast calcifications are common findings on mammography and their frequency increases with the age of the patient. While the majority of microcalcifications that occur are benign, some specific grouped patterns can be caused by malignant disease or high risk lesions1. It is important to differentiate the microcalcifications of benign origin from those that are suspicious, since 55% of non-palpable cancers are diagnosed by the presence of microcalcifications2, and because microcalcifications are the main form of manifestation of ductal carcinoma in situ (DCIS)3. Some of these calcifications not only correspond to pure DCIS, but correspond to the intraductal portion of infiltrating carcinomas4.

Benign calcifications tend to be larger, present a characteristic appearance and do not require magnification. Whereas the suspicious ones tend to be smaller and their characterization should be studied with magnified images.

The density difference between the benign and malignant calcifications is mainly given by the various chemical compounds prevailing in each one. While benign calcifications are composed mainly of calcium oxalate, malignant calcifications are composed predominantly of calcium phosphate. Both types can coexist and their components cannot be determined by mammography, chemical studies being required for these purposes.

The incorporation of digital mammography systems, both direct and indirect, and the use of CAD (computer-aided detection) systems5 has allowed for an improvement in the investigation of microcalcifications. The Vestfold study, in 2008, found a significantly increased detection of DCIS using digital mammography7. It should be noted, however, that even in these systems the requirement of complementary magnified images remains in effect.

Tomosynthesis still exhibits a debatable usefulness in the detection of microcalcifications. Some studies
show detection rates similar to or somewhat lower for tomosynthesis compared with digital mammography$^8,9$. A recent meta-analysis$^{10}$ evaluated the usefulness of this method for classifying microcalcifications according to the BI-RADS categories, demonstrating that tomosynthesis classified the findings similarly to digital mammography in the majority of cases, however, it sub-classified some malignant and premalignant lesions. Therefore, tomosynthesis should still be used with caution in evaluating microcalcifications, and possibly in the future the incorporation of new or complementary descriptors to the BI-RADS lexicon will be required.

The vast majority of microcalcifications are not visible by ultrasound (US) and it only detects large ones or those that are associated with nodules or cysts$^{11}$. On the other hand, even if the calcifications can be demonstrated as echogenic images, it is not possible to adequately characterize them by this method.

Among the main descriptors of calcifications are morphology and distribution, and both must be considered to evaluate the final risk. In the year 2013, the fifth version of the BI-RADS radiological atlas of images and report was published$^{12}$. This new version incorporated changes in the management, nomenclature and descriptors of various lesions and, among these, of calcifications. The aim of this article is to update these descriptors and the BI-RADS categories for microcalcifications, as well as the risk of malignancy associated with each descriptor.

**BI-RADS microcalcification distribution descriptors**

These descriptors refer to the arrangement of the calcifications inside the breast and, relative to the probability of malignancy, it is as important as the morphology$^{12,13}$. In Figure 1 a diagram illustrating the different distribution descriptors used in the BI-RADS categories can be observed.

- **Diffuse distribution:**
  Formerly called “scattered”, these are calcifications randomly distributed within the breast. The punctate and amorphous calcifications in this distribution are usually benign, especially if they are bilateral$^{12}$ (Figura 2).

- **Regional distribution:**
  This pattern describes calcifications in an extensive area, greater than 2 cm in their largest dimension. Because they can cover more than one quadrant their risk of malignancy is low, however, the morphology should be considered to establish the degree of suspicion. A probability of malignancy is described as about 26%$^{12}$ (Figura 3).
• Grouped/clustered distribution:
  This term is used when a few calcifications are found in a small area of tissue. The lower limit for this descriptor are 5 calcifications in 1 cm or when there is a definable pattern. The upper refers to when there are more microcalcifications present within 2 cm. This upper limit is a modification of the 2013 version of BI-RADS. These calcifications can be in the terminal duct lobular units [TDLU], ducts, stroma, masses or on the skin. They require further evaluation with magnified projections and should be grouped in both projections to consider them as such, since, if they only are grouped in one projection, it may correspond to overlapping of calcifications in different positions. They are considered benign or suspicious according to the morphology of each group\textsuperscript{12,14,15} (Figura 4).

• Linear Distribution:
  Calcifications are arranged in a linear path that can branch, suggesting calcium deposits within a duct. A probability of malignancy is described as about 60\%\textsuperscript{12,14,15}. It is worth noting that certain calcifications such as vascular or thick linear may present this distribution, however, they have a characteristically benign morphology (Figura 5).

• Segmental Distribution:
  This distribution pattern suggests the calcium deposit in the ducts and its branches, following the anatomical shape of a breast lobe, i.e. of triangular shape with the tip directed towards the nipple. While it may occur in benign pathology, such as secretory calcifications, its presentation may be due to extensive or multifocal cancer. A probability of malignancy is described as about 62\%\textsuperscript{12,14,15} (Figura 6).
BI-RADS descriptors for microcalcification morphology

These descriptors refer to the morphology of calcifications within the breast tissue. We can divide them into typically benign calcifications, which often do not require magnification or warrant increased monitoring, and in suspicious calcifications requiring magnification for characterization and histological study in the majority of cases.

Typically benign calcifications:
- Vascular calcifications:
  These correspond to calcium deposits in the walls of the mammary arteries. They are usually bilateral, although often more evident to one side. They are displayed as parallel paths or “railroad tracks” corresponding to a tangential view of each vessel wall, which are clearly associated with tubular structures corresponding to the vascular path. Sometimes, when they are initiating or are not clearly related with a vessel, it may be necessary to magnify them. They usually present a serpentine path and may be continuous or discontinuous. They are more common in patients over 50 years of age, with diabetes and chronic renal insufficiency on dialysis, and tend to decrease with the use of hormone replacement therapy. Some international publications have associated them with increased risk of coronary heart disease and cardiovascular disease, their role as a cardiovascular risk marker still being indeterminate (Figura 7).

![Figure 6. Segmental Distribution. Pleomorphic and linear microcalcifications. Stereotactic biopsy showed high grade DCIS.](image)

![Figure 7a. Vascular calcifications. They correspond to parallel calcifications in the vessel walls, typically benign.](image)

b. Vascular calcifications. When they are initiating they are often seen as a linear calcification in the periphery of a tubular structure.
- **Skin (or dermal) calcifications:**
  They correspond to small calcifications of the sebaceous gland, usually associated with inflammatory processes such as chronic folliculitis. They are frequent, usually multiple and pathognomonic. Their morphology is polygonal, sometimes round, with radiolucent center. They measure between 1 and 2 mm and are located more frequently in the inframammary fold, parasternal region, armpit or areola. They are usually visible peripherally in at least one of the two projections, which makes their origin suspicious. Sometimes skin calcifications can give the impression of parenchymal origin, be grouped, in spaces no larger than 5 mm and simulate malignancy. A useful sign in these cases is the “tattoo” sign, in which the group of calcifications does not change its arrangement in the different projections, which corroborates their superficial location. If doubts persist, their location can be confirmed with tangential mammographic projections (Figura 8).

- **Milk of calcium Calcifications:**
  These correspond to small particles of calcium oxalate settling within saccular dilatations of the TDLU (macro or microcysts). More frequent in the peri and postmenopause, usually located in the central and posterior region of the breast, bilaterally. Also called “teacup”. These calcifications are less evident in the craniocaudal projection, being observed as faint and amorphous, and they are visualized better in the strictly lateral projection, where they are observed crescent upper concavity shaped or linear. Since the crescent shape is not always so evident in the lateral projection, it is useful during evaluation to recognize the change of morphology in the different projections (Figura 9). It is suggested to acquire lateral projections first, as movement during compression can reduce visualization of the sediment. If the patient has been moving it may be advisable to wait for 2 to 5 minutes with the patient seated before taking the lateral projections, to ensure that the particles of calcium precipitate. Importantly for better visualization of this sediment, the magnified projection should be taken in strictly lateral position and not oblique.

- **Large linear calcifications:**
  Also known as “secretory” or rod like, they correspond to benign calcifications located in the ducts and associated with ductal ectasia, secretory disease or plasma cell mastitis. They are described in 3% of mammograms. They are linear, smooth calcifications, usually without a radiolucent center as they form in the interior of the duct (intraductal). If calcification occurs in the duct wall (periductal), they could present a radiolucent center. They are usually greater than 0.5 mm and occasionally may branch. Unlike suspicious linear calcifications, these calcifications are usually bilateral and present smooth and regular edges. They generally present a ductal distribution, radiated toward the nipple (Figura 10), and are more common in over 60 year olds. When they are initiating and unilateral they can generate diagnostic doubts.
Popcorn Calcifications: “Popcorn” calcifications are dense, thick, larger than 2-3 mm, which over time tend to coalesce, suggestive of fibroadenomas in involution1,12 (Figura 11). It is usually possible to see the outline of a well-defined node associated with calcification, however, in small fibroadenomas only the calcification can be seen. When they are initiating they may present in the periphery of the nodule.

Dystrophic calcifications: These correspond to a manifestation of fat necrosis in response to a noxa to the breast tissue, which is why the clinical history of the patient is relevant for their diagnosis. They are common after surgery and radiotherapy12. In these cases, they usually occur adjacent to the surgical scar, 3 to 5 years after surgery. It is important to make the differential diagnosis with recurring suspicious calcifications. They may also appear adjacent to implant capsules. They are thick calcifications, usually greater than 1 mm, rough, irregular, which tend to coalesce, sometimes becoming very large and palpable1. The presence of radiolucent areas, which indicate the existence of fat, is important for diagnosis (Figura 12).

Figure 9a. Milk of calcium Calcifications. In craniocaudal projection they are observed faint and amorphous. b. Milk of calcium Calcifications. In strictly lateral magnified projection they are seen crescent shaped. The change in morphology between the two projections is important.

Figure 10 a. Thick linear calcifications. Typically benign, intraductal, originating within a duct. Sometimes branching. Also vascular calcifications are observed. b. Thick linear calcifications. Typically benign, periductal, with radiolucent center, originating in the duct wall.
Round calcifications / punctate:
As the name suggests, these calcifications are round, they may present different sizes and have their origin at the acinar or lobular level. They are called round when they are greater than 0.5 mm and punctate when they are smaller than this size. They usually correspond to calcium oxalate deposits and are more common in over 40 year olds. When they are isolated, diffuse and small they are considered benign (Figura 13). When they are mostly grouped they are assigned to the BI-RADS 3 category²⁰ and deserve short-term monitoring (6 months) or comparison with previous examinations (Figura 14). If the group is of recent appearance, more numerous than in previous controls, of linear or segmental distribution or adjacent to a known cancer it may be advisable to perform a histological study¹².

**Figure 11.** Popcorn calcifications: a nodule with coarse calcifications, some confluent, is observed. Presumptive diagnosis: reactionary fibroadenoma.

**Figure 12.** Dystrophic calcifications. They are thick calcifications, with radiolucent areas, in relation to an area of structural distortion, in a patient operated for invasive carcinoma.

**Figure 13.** Round calcifications. Scattered, benign aspect.

**Figure 14 a.** Round calcifications. Grouped, warranting an initial monitoring in 6 months. b. Round calcifications. Another group of presumably benign round, grouped calcifications.
• Ring Calcifications:
The calcifications called “eggshell” and “radiolucent centered” were eliminated in the 2013 version BI-RADS Atlas and incorporated as typically ring-like benign calcifications. They correspond to encapsulated cystic lesions containing fat in liquid state, although they have also been described on the surface of simple cysts. Initially they are seen in mammography as radiolucent round or oval lesions that over time acquire a calcified spherical and thin surface, through which a radiolucent center is seen. This thin deposit of calcium usually has a thickness of less than 1 mm seen on the edge (Figura 15). They range in size from a few millimeters to centimeters. They can occur anywhere in the breast, but are more common in superficial location. They are usually associated with a history of trauma or surgery. In voluminous breasts they may occur spontaneously.

• Suture calcifications:
These represent calcium deposited in the suture material. They are linear or tubular calcifications that may present knots. These calcifications are more common in patients who have undergone radiotherapy possibly because the damage induced by radiation alters the healing and delays the reabsorption of catgut, providing a matrix for calcium deposit (Figura 16).

Figure 16. Suture calcifications. Calcifications forming knots, typically benign, are observed. Adjacent to these it is possible to see some small ring calcifications.

Calcifications of suspicious morphology
• Coarse heterogeneous calcifications:
Also known as rough, heterogeneous, they are irregular and defined calcifications which tend to coalesce. Measuring more than 0.5 mm, i.e., more than the pleomorphic calcifications but less than the dystrophic calcifications (Figura 17). These may be located in the breast stroma or ducts. Most of these calcifications originate in benign lesions such as reactionary fibroadenomas, areas of fibrosis or trauma. In the latter case they correspond to dystrophic calcifications in evolution. When they are multiple and bilateral they are usually considered benign, however, one lone group presents a positive predictive value of close to 15%, so it is considered within the 4B category.

Figure 15 a. Ring calcifications. Formerly called oil cysts, these correspond to rounded lesions, of low density, with fine initial peripheral calcifications in a patient with a history of local trauma. b. Ring calcifications. Spherical lesion with a thin calcified surface, through which a radiolucent center is seen.
• Amorphous calcifications:
  Also called “powder”, “cloud” or “cottony” they correspond to such small calcifications (less than 0.1 mm), it is not possible to count them nor determine their shape. Hence the name “amorphous” (shapeless) (Figura 18). To categorize them as amorphous these calcifications should not decant in the strictly lateral projections, as in that case they would correspond to milk of calcium calcifications. Many of them are benign, such as those originated in fibrocystic changes, especially when they are diffuse and bilateral\(^{23}\). However, when they are grouped, they present a segmental or linear distribution\(^{12}\). They may be due to high-risk lesions or malignant etiology, which justifies indications for histological studies. The positive predictive value is approximately 20%, so they are included in the 4B category\(^{12}\).

• Fine pleomorphic calcifications:
  Also called “crushed stone”. They correspond to calcifications of different shapes and sizes, angled, heterogeneous, with a size between 0.5 and 1 mm (Figura 19), smaller than the coarse heterogeneous calcifications. While their predictive value of 29% is higher than the amorphous and coarse heterogeneous calcifications, they are included in the BI-RADS 4B category and have histological studies indicated\(^{12,14,15,22}\).

**Figure 17.** a. Heterogeneous calcifications. They are clustered calcifications, irregularly shaped, defined, with a tendency to coalesce. Digital Stereotactic biopsy: fibroadenomatoid hyperplasia with stromal sclerosis and dystrophic calcifications associated with ductal ectasia and chronic periductal mastitis. b. Heterogeneous calcifications. Coarse, thick, irregular calcifications. Digital stereotactic biopsy: hyalinized fibroadenoma.

**Figure 18.** Amorphous microcalcifications. Group of faint microcalcifications, amorphous. Digital stereotactic biopsy: Flat atypia and sclerosing adenosis.

**Figure 19a.** Fine pleomorphic microcalcifications. They are irregular calcifications, of different shapes and sizes, suspicious appearance. b. Fine pleomorphic microcalcifications. Associated with a dense asymmetry and structural distortion. Digital stereotactic biopsy: High-grade DCIS with comedocarcinoma type necrosis and cancerization of lobules.
• Fine linear or branched calcifications:
  These correspond to small calcifications, less than 0.5 mm, thin, linear, usually discontinuous and with irregular edges, which originate in calcified necrotic debris within a duct compromised by carcinoma, i.e., they present calcium molds in an irregular duct. They may branch in different directions forming ‘letters’ (L, V, Y, X) (Figura 20).
  Of the suspicious calcifications, these are the ones that have the highest positive predictive value for malignancy (70%) and correspond to BI-RADS 4C category\textsuperscript{12,14,15,22}. When these microcalcifications are new and present a segmental distribution they can be considered within the BI-RADS 5 category\textsuperscript{12}.

Figure 20. Thin, linear and branched microcalcifications. Stereotactic biopsy showed high grade DCIS with necrosis.

Classification of microcalcifications in BI-RADS categories

According to the different descriptors and degrees of suspicion of malignancy mentioned, it is possible to assign a BI-RADS category to each type of microcalcification\textsuperscript{12}. When there is an association of different types of descriptors, either distribution or morphology, the final BI-RADS category will be that of those microcalcifications of higher grade.

Unlike the 2003 version BI-RADS Atlas, in 5th Edition 2013, the 2 categories marked as suspicious (calcifications with intermediate degree of suspicion and calcifications with high probability of malignancy) where eliminated for a single category: calcifications with suspicious morphology, i.e., one category replaces the previous 2 given that clinical studies at this time have shown very small differences in the risk of malignancy.

Moreover, since the 4th edition of the BI-RADS Atlas, several articles have been published supporting the decision to optionally and internally subdivide the BI-RADS 4 category into 3 subcategories, in order to properly represent the wide variety of lesions that are subjected to interventional procedures and therefore to the wide margin that have the probability of malignancy. These 3 subcategories correspond to categories 4A (> 2% to ≤ 10%), 4B (> 10% to ≤ 50%) and 4C (> 50% to <95%).

The classification of the microcalcifications is summarized in Table 1.

| Table 1. Classification of calcifications according to BI-RADS categories. |
|-----------------------------|----------------------|
| **Calcification type**      | **Category**         |
| Vascular calcifications     | BI-RADS 2            |
| Skin calcifications         | BI-RADS 2            |
| Milk of calcium calcifications | BI-RADS 2         |
| Thick linear calcifications | BI-RADS 2            |
| Popcorn calcifications      | BI-RADS 2            |
| Dystrophic calcifications   | BI-RADS 2            |
| Round, scattered or isolated calcifications | BI-RADS 3 |
| Ring calcifications         | BI-RADS 3            |
| Suture calcifications       | BI-RADS 3            |
| Round grouped calcifications| BI-RADS 3            |
| Coarse, rough, heterogeneous calcifications | B |
| Amorphous calcifications    | BI-RADS 4            |
| Fine pleomorphic calcifications | B |
| Linear or branched linear calcifications | C |
| Linear and new branching linear and segmental distribution calcifications | BI-RADS 5 |

Stability of microcalcifications

In a study published by Lev-Toaff et al.\textsuperscript{24}, stability over time of suspicious microcalcifications in 105 patients was revised. It was concluded that the temporal stability of microcalcifications significantly decreases the risk of an invasive carcinoma, but not necessarily of a carcinoma in situ. Therefore, if a group of microcalcifications give the impression of suspicious characteristics, they have indication for histological studies regardless of their stability over
time. Moreover, the fact that microcalcifications appear or increase does not necessarily imply malignancy, but is one of the criteria to suggest their study.

It is worth noting that the monitored microcalcifications classified as BI-RADS 3 must be assessed with magnified projections in each control until the decision to change the BI-RADS category.

Conclusions
Proper management of the distribution descriptors and morphology of microcalcifications will allow an optimal BI-RADS categorization and a resulting management based on these findings. This becomes important in the investigation in the early stages of malignancies presenting microcalcifications such as DCIS. This process of integration, from the characterization, categorization and management indications, may require the agreed analysis of experts in the more complex cases. Given the constant technological changes, it is essential to be in constant review of new diagnostic possibilities in order to determine how these integrate with current techniques and knowledge.

Ethical responsibilities
Protection of people and animals. The authors declare that no experiments have been performed on humans or animals for this investigation.

Confidentiality of data. The authors declare that they have followed the protocols of the workplace regarding the publication of patient data.

Privacy rights and informed consent. The authors declare that patient data does not appear in this article.

Conflict of interests
The authors declare no conflict of interest.

Bibliography